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THE IMPACT OF MICROPLASTICS AND NANOPLASTICS ON HUMAN HEALTH: A FOLLOW-UP STUDY FOCUSING ON ENDOCRINE, NERVOUS, AND IMMUNE SYSTEMS

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Abstract: *Plastic production has surged over recent years, leading to widespread environmental contamination by microplastics (MPs) and nanoplastics (NPs). These particles, due to their small size and persistence, can enter the human body via ingestion, inhalation, or dermal contact and have been detected in various organs including the lungs, liver, bloodstream, and even cerebrospinal fluid. This study examines the impact of microplastics and nanoplastics (M-NPLs) on three critical physiological systems: the endocrine, nervous, and immune systems. Despite the essential roles these systems play in human health, their vulnerability to M-NPLs remains underexplored. This paper reviews exposure pathways, translocation mechanisms, and how MPs/NPs interact with these systems to induce hormonal disruption, neuroinflammation, and immune dysregulation. Given their ability to cross biological barriers, M-NPLs may pose significant systemic health risks. However, current limitations in detection methods and the lack of long-term human data hinder accurate risk assessment. These findings highlight the urgent need for targeted research to better understand the systemic toxicity of M-NPLs.*

Keywords: plastic particles, systemic toxicity, human health, neurotoxicity, endocrine disruption

1. Introduction

Over the past seven decades, plastic production and consumption have increased exponentially, leading to widespread environmental accumulation. In 1950, global plastic production stood at approximately 2 million tons; by 2023, it had surpassed 400 million tons [1]. Plastic's versatility, sterility, and low cost have made it indispensable in numerous sectors – from food packaging and construction to healthcare and electronics.

However, improper disposal and limited recycling management have resulted in persistent environmental plastic waste. Through physical, chemical, and biological degradation processes, this plastic waste breaks down into progressively smaller particles: macroplastics (> 1 cm), mesoplastics (1 – 10 mm), microplastics (1 – 1000 μm), and nanoplastics (1 – 1000 nm) [2].

MPs and NPs raise the greatest concern, as are small enough to enter biological systems and cross cellular barriers. Today, their presence in the air we breathe, the water we drink, the food we eat, and human tissues is well-documented [3].

Recent studies highlight the toxic potential of M-NPLs, with mechanism including oxidative stress, inflammation, immune dysregulation, and endocrine disruption [4].

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In our previous study, we explored their impact on the digestive, respiratory, and cardiovascular system [5]. However, emerging research suggests that other major systems, including the nervous, endocrine, and immune systems are also vulnerable, given their complexity and sensitivity to foreign substances. For instance, NPs can cross the blood-brain barrier, raising concerns about neuroinflammation and neurotoxicity. Similarly, the endocrine system is known to be susceptible to plastic-associated chemicals like bisphenol A and phthalates, which may interfere with hormone signalling. The immune system can also be affected through persistent inflammatory responses and altered cytokine production [6].

This study aims to extend our previous work [5] by focusing specifically on the effects of M-NPLs on the nervous, endocrine and immune systems. These systems are essential to human health but remain understudied in the context of plastic exposure. To address this gap, the study draws on a targeted review of scientific literature published between 2020 and 2025, incorporating peer-reviewed articles, in vitro and in vivo experiments, as well as the limited human data currently available.

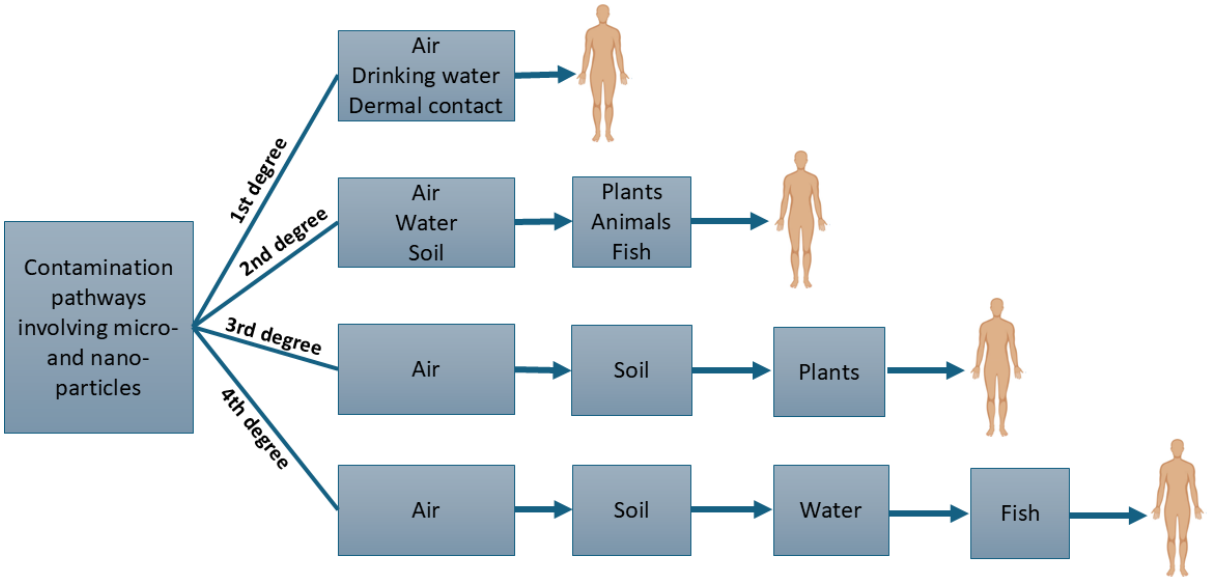

Figure 1: Contamination pathways involving M-NPLs

2. Exposure and contamination pathways

M-NPLs can enter the human body through various exposure routes, which differ based on the number of intermediary stages in the distribution chain and the time required for contaminants to reach the human host. The exposure pathways can be classified into four degrees, depending on their complexity and speed (Figure 1):

- First-degree contamination pathway: Direct exposure occurs rapidly, with minimal intermediaries. Contaminants move directly from plastics or from a primary environmental source, such as air or drinking water into the human body.
- Second degree contamination pathway: Contaminants are first transferred to a primary medium (air or water), then to the secondary sources such as vegetation, fruits, vegetables, or animals, before ultimately being ingested or inhaled by humans.
- Third-degree contamination pathway: Exposure follows a more extended route: contaminants move from a primary medium (air or water) to a secondary medium (soil), and then to third compartment such as food-producing organism (plants or animals), before

reaching the human body.

- Fourth-degree contamination pathway: The most complex and delayed exposure route involves multiple stages. For example, airborne plastics (first compartment) settle into the soil (second compartment), then contaminate aquatic environments (third compartment), and accumulate in aquatic organism such as fish, seafood or water plants (fourth compartment), which are eventually consumed by humans [7].

The complexity of the contamination pathway significantly influences the quantity and bioavailability of harmful substances reaching the human body. Notably, shorter contamination chains may deliver higher concentration of M-NPLs, as there is less opportunity for degradation or filtration.

3. Distribution and Translocation of M-NPLs in human body

Humans are primarily exposed to M-NPLs through oral intake, inhalation and dermal contact. Ingestion occurs via contaminated food and beverages, with items such as shellfish, bottled water, and take-out packaging being notable sources. Inhalation involves air-borne M-NPLs derived from synthetic materials, industrial emissions, nd dust. Dermal exposure is less common but can occur through cosmetics, personal care products, and medical devices, especially when the skin is damaged (Figure 2). Once internalized, MPs and especially NPs can translocate beyond initial exposure sites. Once inside the body, some plastic particles are excreted via physiological processes, such as sweating, urination, or defecation, while other persists and accumulate in tissues. They have been detected in various organs, including the lungs, liver, blood, kidneys, spleen, placenta, or even heart [6,8]. Their distribution is influenced by size, surface charge, hydrophobicity, and the presents of adsorbed chemicals or proteins [9]. Chronic accumulation may lead to persistent inflammation, oxidative stress, or disruption of local cell functions, which may lead to the development of various diseases (Figure 2) [10].

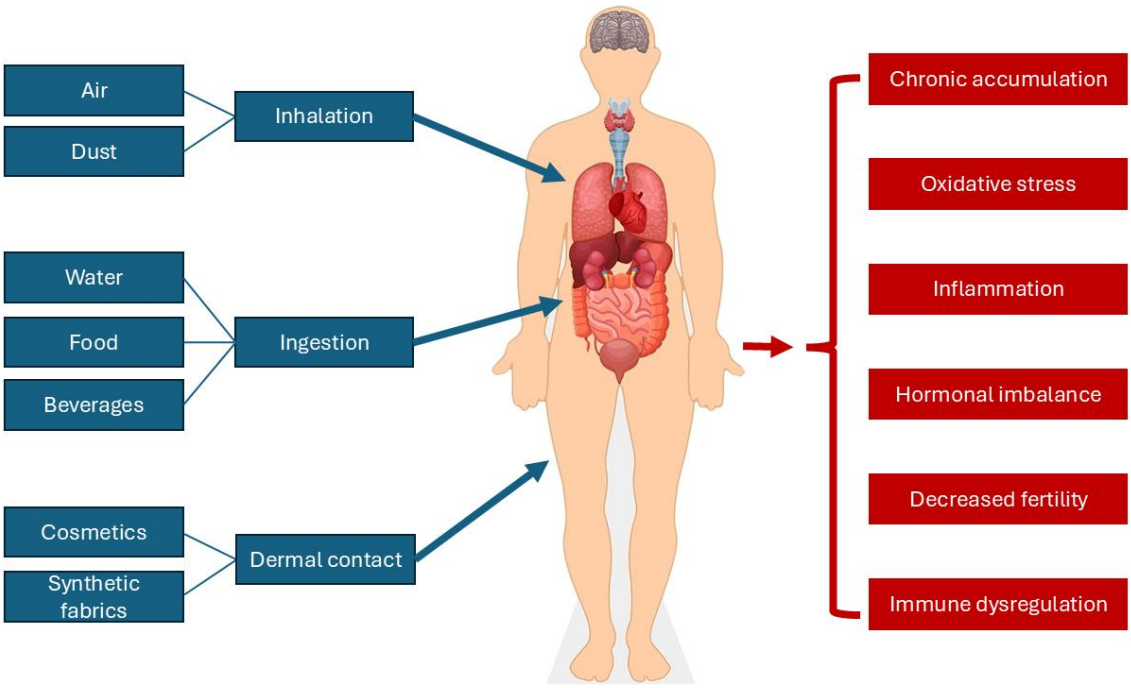

Figure 2: Pathways of human exposure to M-NPLs and associated risks

4. Systemic toxicity of M-NPLs

4.1 Effects on the endocrine system

The endocrine system is particularly sensitive to the chemical contaminants due to its reliance on precise hormonal regulation. M-NPLs pose a significant threat to endocrine health, not only due to their physical presence but also because they act as carriers for endocrine-disrupting chemicals. The substances can mimic, block or interfere with natural hormones, leading to systemic hormonal imbalance.

Experimental studies have shown that exposure to M-NPLs can disrupt the synthesis, transport, metabolism, and receptor activity of key hormones [11].

- Thyroid:

Previous published studies have shown that M-NPLs can interfere with thyroid hormone synthesis and signalling, particularly affecting the hypothalamic-pituitary-thyroid axis. Altered levels of T3 and T4 hormones have been observed in animal models, suggesting disrupted metabolic regulation.

- Reproductive glands:

In reproductive systems, exposure to M-NPLs has been associated with reduced sperm quality, testosterone suppression, ovarian dysfunction, menstrual irregularities, and adverse effects offspring's lipid metabolism and reproductive system. However, current limitations in detection methods may underestimate the true extend of M-NPLs - related reproductive toxicity. Therefore, advancements in analytical techniques are essential to accurately assess their impact on reproductive health [12].

- Adrenal glands:

The adrenal glands, responsible for stress and metabolic hormones like cortisol and aldosterone, may also be affected. Early research in rodents has indicated that NPs can potentially alter cortisol output and contribute to immune and metabolic dysregulation. Persistent low-level exposure to plastic-associated chemicals may lead to chronic stress response or altered blood pressure regulation.

- Pancreas:

The pancreas plays a central role in glucose metabolism, particularly through the β-cells of the islet of Langerhans. M-NPLs may impair insulin secretion or promote insulin resistance, possibly via oxidative stress pathways. In piglets, it was shown that MPs may increase blood insulin concentrations and lipid levels, which may increase the risk of insulin resistance and pancreatitis.

- Pituitary and pineal gland:

Though less studied, the pituitary gland – which controls the endocrine organs via hormones like FSH, LH, TSH, and ACTH – could also be vulnerable to upstream disruption. M-NPLs may interfere with hypothalamic-pituitary communication, resulting in secondary effects on the thyroid, adrenals, and gonads. The pineal gland, which regulates melatonin and circadian rhythms, may also be indirectly affected if plastic accumulate in brain tissue, although this remains speculative and has not been proved until now.

The endocrine system is highly susceptible to disruption by M-NPLs due to their role as physical particles and chemical vectors. While research has focused largely on the thyroid and reproductive systems, early evidence suggests that the adrenals, pancreas, and central regulatory glands may also be at risk. The effects of M-NPLs on endocrine health may be non-linear, dose-independent, and slow to manifest, making them difficult to detect using traditional toxicology models. Comprehensive studies across all endocrine organs are essential to fully understand the scope of plastic-related hormonal dysfunction [11].

4.2 Effects on the nervous system

The nervous system, particularly the central nervous system (CNS), is highly vulnerable to xenobiotic compounds, including M-NPLs. One of the most concerning characteristics of NPs is their

ability to cross the blood-brain barrier (BBB), a selective permeable membrane designed to protect the brain from harmful substances. Due to their small size, surface charge and protein corona formation, NPs can cross the BBB via transcytosis or endocytic mechanism and gain access to brain tissue.

Once with in the CNS, NPs may induce neuroinflammation, oxidative stress, and mitochondrial dysfunction. These effects are typically mediated by the generation of reactive oxygen species, which disrupts neural cell homeostasis and may lead to cell death. In vitro studies have demonstrated that polystyrene nanoparticles (PSNPs) can cause neuronal membrane disruption, reduce synaptic activity and impar neurotransmitter signalling, including acetylcholine and dopamine pathways [13].

Experimental research on animal models has revealed behavioural and cognitive impairments following M-NPLs exposure. Rodents expose to PSNPs showed signs of anxiety, reduced memory performance, and motor deficits, suggesting direct impacts on neurological functions. Moreover, zebrafish and mice exposed to MP-NPs showed altered expression of genes involved in neurodevelopment, inflammation, and apoptosis [13,14].

Although human data are still limited, recent findings have detected plastic particles in human cerebrospinal fluid, suggesting that systemic circulation of M-NPLs can reach the brain. Given the long-term persistence of plastics in the body and their potential cumulative effects, there is growing concern about the role of M-NPLs in neurodegenerative conditions, such as Alzheimer's and Parkinson's diseases [14,15].

4.3. Effects on the immune system

The immune system plays a critical role in defending the body against pathogens, maintaining tissue homeostasis, and resolving inflammation. M-NPLs, due to their persistent and bioactive nature, are recognized as potential disruptors of immune function. Their interaction with immune cells can result in chronic low-grade inflammation, immunosuppression, or even autoimmune-like responses, depending on exposure levels, particles characteristics, and host susceptibility.

- Immune activation and inflammation:

Both in vitro and in vivo studies have shown that M-NPLs can activate macrophages, dendritic cells, and epithelial cells, prompting the release of pro-inflammatory cytokines such as IL-6, TNT-α, and IL-1β. This immune stimulation is often mediated by the recognition of plastic particles as foreign bodies and exacerbated by adsorbed contaminants like heavy metals, polycyclic aromatic hydrocarbons, or microbial toxins on their surface. Prolonged immune activation may contribute to tissue damage, fibrosis, or local immune exhaustion [16].

- Immune suppression and dysregulation:

In contrast to pro-inflammatory effects, M-NPLs have also shown to suppress immune responses. In animal models, high doses of plastics reduced the proliferation and function of T-cells and B-cells, impairing adaptive immunity. Suppression of natural killer (NK) cell activity has also been documented, potentially compromising antitumor and antiviral defence mechanisms. These effects may be particularly concerning in immunocompromised individuals or populations with chronic exposure [17].

- Gut-associated immune impact:

Due to the predominance of oral exposure, the gut-associated lymphoid tissue represents a primary interface for M-NPLs interaction with the immune system. While direct evidence in humans is limited, experimental studies in rodents and zebrafish have demonstrated that M-NPLs can impair intestinal barrier integrity, enhance mucosal permeability, and trigger inflammatory cell infiltration with gut tissues. Such disruptions may contribute to

the onset of immune-related gastrointestinal disorders and facilitate systemic inflammation by allowing translocation of bacteria or endotoxins into circulation [18].

- Potential autoimmune implications:

While direct links between M-NPLs and autoimmune diseases are still speculative, some experimental data suggests that chronic plastic exposure could disturb immune tolerance. The prolonged presence of plastic particles in tissues may lead to immune sensitisation, autoantigen presentation, and aberrant immune memory, thereby increasing the risk for conditions such as rheumatoid arthritis, lupus, or inflammatory bowel disease [19]. Mechanistically, immune disruption by M-NPLs appears to involve oxidative stress, mitochondrial damage, and pattern recognition receptor activation. As a result, the immune system is highly susceptible to the pro- and anti- inflammatory effects of M-NPLs. Currently, there is limited data on the long-term effects of low-dose exposure to M-NPLs on the human immune system. Future research should focus on these realistic exposure scenarios to better understand their cumulative impact on immune function across the general population

5. Conclusion

This study provides novel insights into the widespread presence and underexplored health risks associated with M-NPLs, by shifting the focus beyond the extensively studied systems such as digestive and cardiovascular systems. M-NPLs have become omnipresent in the environment, and an increasing number of studies have confirmed their accumulation within the human body. Their small size, ability to cross biological barriers, and capacity to carry toxic substances raise serious concerns about their long-term impact on human health. Recent findings showed that M-NPLs significantly disrupts endocrine, nervous, and immune systems, including perturbations in hormonal regulation, neurological impairments, and modulation of immune responses. These disruptions may contribute to chronic inflammation, metabolic disorders, neurodegeneration, and endocrine dysfunction. The originally of these this work lies in anticipating potential effects on human systems through the synthesis of results obtained from animal models and in vitro studies. This strategy enables a more informed understanding of the possible human health implications, despite the critical lack of long-term, low-dose human exposure data. Consequently, this study underscores the urgent need for the development of advanced detection methods, realistic exposure models, and long-term human studies. Such efforts are essential for accurately assessing the health risks posed by M-NPLs.

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